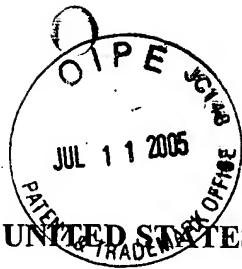


OREX.009A



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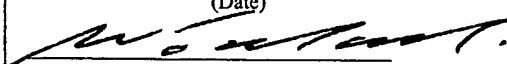
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Gadde et al.
Appl. No. : 10/440,404
Filed : May 19, 2003
For : **METHOD FOR TREATING
OBESITY**
Examiner : Dwayne C. Jones
Group Art Unit: 1614

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: United States Patent and Trademark Office, P.O. Box 2327, Arlington, VA 22202, on

May 17, 2005

(Date)


Sam K. Tahmassebi, Reg. No. 45,151

DECLARATION OF KISHORE M. GADDE SUBMITTED UNDER 37 C.F.R. § 1.132

United States Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

I, Kishore M. Gadde, M.D., do hereby declare:

1. I am currently a physician in the Department of Psychiatry at Duke University Medical Center.
2. I have 15 years of experience treating and studying individuals with psychiatric disorders, such as major depression, bipolar disorder, and schizophrenia.
3. I have 7 years experience in treating and studying obese individuals.
4. In the course of my practice, I have encountered numerous individuals who became obese as the result of treatment with psychotropic medications.
5. One such individual was a 30 year old female with a diagnosis of bipolar disorder. This individual gained 56 lbs while receiving olanzapine and valproate over 5 years. Since her mental illness was effectively controlled, these medications were continued despite significant weight gain. She was clinically obese with a BMI of 33.8 kg/m².
6. In an effort to assist in weight reduction, bupropion was added at 150 mg/d while olanzapine and valproate were continued. When the bupropion dose was raised to 300 mg/d, the patient reported feeling hyperactive; hence, the dose was reduced back to 150 mg/d. After 6

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months, the patient lost 23.6 lb. However, while continuing to receive bupropion, the patient regained 10.6 lb over the next 10 months.

7. At this point, zonisamide was added to her medication regimen at 100 mg/d and the dose was increased to 200 mg/d after two weeks. The patient lost 15 lb over the next 4 months and reported no adverse effects. At the same time, she remained free of bipolar disorder symptoms.

8. The case detailed above illustrates two advantages of the combination therapy of bupropion and zonisamide: 1) Although bupropion helped in decreasing weight gain resulting from olanzapine and valproate, the patient could not take a higher dose (300-400 mg/d) of bupropion because of precipitation of hypomanic symptoms. 2) Zonisamide helped in *further* offsetting weight gain associated with olanzapine and valproate after the patient lost weight initially with bupropion and then regained some of the lost weight.

9. The effect of the combination of zonisamide and bupropion was synergistic. Although bupropion initially caused weight loss, this effect reached a plateau after 6 months and was reversed after that. The addition of zonisamide was instrumental in continuing the weight loss and maintaining the lower weight.

10. This result was surprising because I did not expect the addition of zonisamide to ensure a sustained weight loss that was not achieved with bupropion alone.

11. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

Respectfully submitted,

Dated: 4/26/05

By: /Kishore M. Gadde, MD/
Kishore M. Gadde, M.D.